* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:42:38 ON 24 MAY 2005

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C
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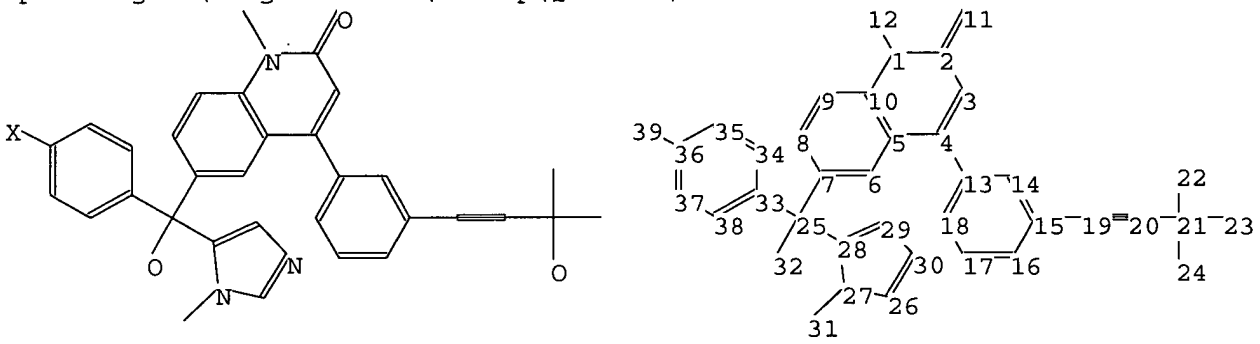

ring nodes :
1 2 3 4 5 6 7 8 9 10 13 14 15 16 17 18 26 27 28 29 30 33 34 35 36 37 38
ring/chain nodes :
11 12 19 20 21 22 23 24 25 31 32 39
ring/chain bonds :
1-12 2-11 4-13 7-25 15-19 19-20 20-21 21-22 21-23 21-24 25-28 25-32 25-33 27-31 36-39
ring bonds :
1-2 1-10 2-3 3-4 4-5 5-6 5-10 6-7 7-8 8-9 9-10 13-14 13-18 14-15 15-16 16-17 17-18 26-27 26-30 27-28 28-29 29-30 33-34 33-38 34-35 35-36 36-37 37-38
exact/norm bonds :
4-13 7-25 15-19 19-20 20-21 21-22 21-23 25-28 25-33 36-39
exact bonds :
1-2 1-10 1-12 2-3 2-11 3-4 4-5 21-24 25-32 26-27 26-30 27-28 27-31 28-29 29-30
normalized bonds :
5-6 5-10 6-7 7-8 8-9 9-10 13-14 13-18 14-15 15-16 16-17 17-18 33-34 33-38 34-35 35-36 36-37 37-38
isolated ring systems :
containing 1 : 13 : 26 : 33 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 32:CLASS 33:Atom 34:Atom 35:Atom 36:Atom

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L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
L3            5 SEA SSS FUL L1

=> file ca


=> s l3
L4            2 L3

=> d ibib abs hitstr 1-2
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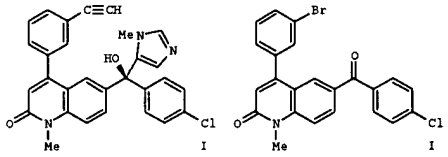
L4 ANSWER 1 OF 2 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 141:207124 CA
TITLE: Streamlined Processes for the Synthesis of a Farnesyl Transferase Inhibitor Drug Candidate
AUTHOR(S): Andresen, Brian M.; Couturier, Michel; Cronin, Brian; D'Occhio, Michael; Ewing, Marcus D.; Guinn, Mark; Hawkins, Joel M.; Jasys, V. John; LaGreca, Susan D.; Lyssikatos, Joseph P.; Moraski, Garrett; Ng, Karl; Raggon, Jeffrey W.; Stewart, A. Morgan; Tickner, Derek L.; Tucker, John L.; Urban, Frank J.; Vazquez, Enrique; Wei, Lulin
CORPORATE SOURCE: Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Organic Process Research & Development (2004), 8(4), 643-650
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:207124
GI

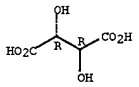


AB As part of a fast-paced oncol. program, quinolinone I was discovered and developed as a potent inhibitor of farnesyl transferase for the treatment of cancer. The initial synthesis, which suffered from a lengthy linear sequence and a late-stage chromatog. resolution, was deemed not amenable to large-scale production While investigating alternate routes to address these issues, the original synthesis was successively improved and streamlined. This enabled route supplied the timely production of drug substance required to support early toxicol. and clin. studies. Several iterations of the process were made, and as a result of these improvements, an efficient four-step sequence was developed for the synthesis of I as its D-tartrate, starting from readily available outsourced intermediate II in 26% overall yield, including a classical resolution The key features of the synthesis include a Castro-Stevens coupling, an imidazole Grignard addition, and a concomitant classical resolution/final salt formation with D-(-)-tartaric acid.

IT **501421-81-4P 501421-87-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-[(4-chlorophenyl)hydroxy(3-methyl-3H-imidazol-4-yl)methyl]-

L4 ANSWER 1 OF 2 CA COPYRIGHT 2005 ACS on STN (Continued)

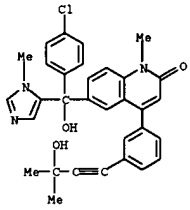
Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 2 CA COPYRIGHT 2005 ACS on STN (Continued)
4-(3-ethynylphenyl)-1-methyl-1H-quinolin-2-one, a farnesyl transferase inhibitor drug candidate)

RN 501421-81-4 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl- (9CI) (CA INDEX NAME)

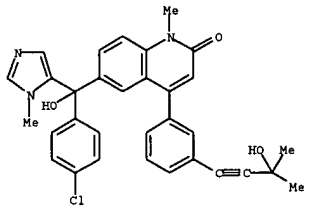


RN 501421-87-0 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl-, (+)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 501421-86-9
CMF C32 H28 Cl N3 O3

Rotation (+).



CM 2

CRN 87-69-4
CMF C4 H6 O6

L4 ANSWER 2 OF 2 CA COPYRIGHT 2005 ACS on STN

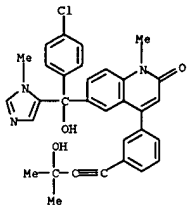
ACCESSION NUMBER: 138:239688 CA
TITLE: Enantiomers of 6-[(4-chlorophenyl)-hydroxy-(3-methyl-3H-imidazol-4-yl)-methyl]-4-[3-(3-hydroxy-3-methylbut-1-ynyl)-phenyl]-1-methyl-1H-quinolin-2-one and salts thereof, useful in the treatment of cancer
INVENTOR(S): Guinn, Mark R.; Guhan, Subramanian Sam; Ng, Karl K.; Ewing, Marcus Douglas; Tickner, Derek L.; Pouwer, Kees; Meltz, Clifford N.; Li, Bryan
PATENT ASSIGNEE(S): Osi Pharmaceuticals, Inc., USA; Pfizer Products, Inc.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003021355	A1	20030313	WO 2002-US27464	20020829
WO 2003021355	C2	20030710		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003114487	A1	20030619	US 2002-228657	20020827
US 6740757	B2	20040525		
US 2004192727	A1	20040930	US 2004-824034	20040414
PRIORITY APPLN. INFO.:			US 2001-315740P	P 20010829
			US 2002-228657	A3 20020827

AB This invention relates to the enantiomers of 6-[(4-chlorophenyl)hydroxy(3-methyl-3H-imidazol-4-yl)methyl]-4-[3-(3-hydroxy-3-methylbut-1-ynyl)phenyl]-1-methyl-1H-quinolin-2-one, prodrugs thereof, and pharmaceutically acceptable salts and solvates of said compds. and said prodrugs, that are useful in the treatment of hyperproliferative diseases, such as cancers, in mammals. The invention also relates to processes for the large-scale production of enantiomerically pure or optically enriched (+)- or (-)-6-[(4-chlorophenyl)hydroxy(3-methyl-3H-imidazol-4-yl)methyl]-4-[3-(3-hydroxy-3-methylbut-1-ynyl)phenyl]-1-methyl-1H-quinolin-2-one enantiomers from a mixture containing two enantiomers using continuous chromatog. with a liquid mobile phase containing ≥1 polar solvent and a solid chiral stationary phase based on a derivatized amylosic or cellulosic polysaccharide. The invention further relates to the L-(+)-tartaric acid or (S)-(-)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate salts of (+)-6-[(4-chlorophenyl)hydroxy(3-methyl-3H-imidazol-4-yl)methyl]-4-[3-(3-hydroxy-3-methylbut-1-ynyl)phenyl]-1-methyl-1H-quinolin-2-one and their manufacture

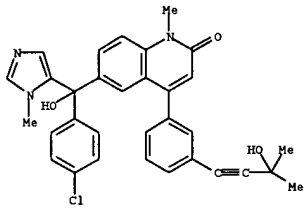
IT **501421-81-4P**
RL: CPS (Chemical process); IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(separation of enantiomers of [(chlorophenyl)hydroxy(methylimidazolyl)methyl][(hydroxymethylbutynyl)phenyl]methylquinolinone for treatment of cancer)

L4 ANSWER 2 OF 2 CA COPYRIGHT 2005 ACS on STN (Continued)
RN 501421-81-4 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl- (9CI) (CA INDEX NAME)



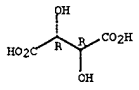
IT **501421-85-8P 501421-86-9P 501421-87-0P 501421-88-1P**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(separation of enantiomers of [(chlorophenyl)hydroxy(methylimidazolyl)methyl][(hydroxymethylbutynyl)phenyl]methylquinolinone for treatment of cancer)
RN 501421-85-8 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



RN 501421-86-9 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl-, (+)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 2 CA COPYRIGHT 2005 ACS on STN (Continued)

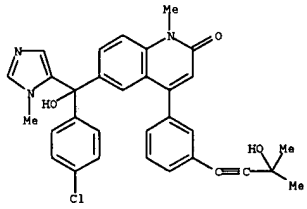


RN 501421-88-1 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl-, (+)-, compd. with (1S)-[1,1'-binaphthalene]-2,2'-diylbis[diphenylphosphine] (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 501421-86-9
CMF C32 H28 Cl N3 O3

Rotation (+).



CM 2

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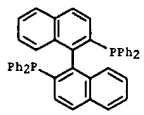
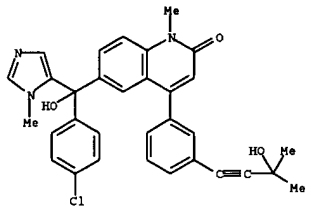


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CA COPYRIGHT 2005 ACS on STN (Continued)

Rotation (+).

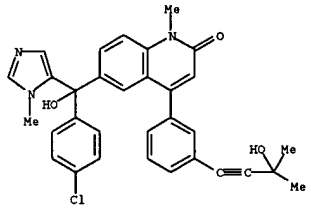


RN 501421-87-0 CA
CN 2(1H)-Quinolinone, 6-[(4-chlorophenyl)hydroxy(1-methyl-1H-imidazol-5-yl)methyl]-4-[3-(3-hydroxy-3-methyl-1-butynyl)phenyl]-1-methyl-, (+)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 501421-86-9
CMF C32 H28 Cl N3 O3

Rotation (+).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

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L5 HAS NO ANSWERS
L5              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


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=> s l6/com
L7            0 L6/COM

=> d his

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     FILE 'REGISTRY' ENTERED AT 14:43:00 ON 24 MAY 2005
L1              STRUCTURE UPLOADED
L2            2 S L1 SAM
L3            5 S L1 FULL

     FILE 'CA' ENTERED AT 14:43:26 ON 24 MAY 2005
L4            2 S L3
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10/824,034

STN INTERNATIONAL LOGOFF AT 14:49:24 ON 24 MAY 2005